L6 ANSWER 1 OF 1 ZCA COPYRIGHT 2007 ACS on STN
AN 130:267450 ZCA Full-text
TI Preparation of ethynylpyrimidine derivatives as tyrosine kinase inhibitors and their pharmaceutical uses
IN Kitano, Yasunori; Kawahara, Eiji; Takayanagi, Hisao; Suzuki, Takeshi; Ohya, Atsushi; Hara, Hiroto
PA Mitsubishi Chemical Industries Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 235 pp.
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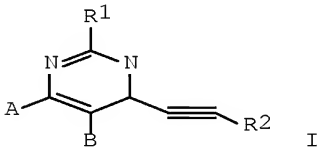

I

AB The derivs. I [A, B = NO2, (CH2)n (n = 0, 1), NR3R4 (R3, R4 = H, C1-5 alkyl which may be substituted with CO2H or C1-5 alkoxycarbonyl) or AB = CX1:CX2CX3:CX4 [X1-X4 = H, halo, NO2, OR (R = C3-8 cycloalkyl which may contain O, C1-5 alkyl which may be substituted with C1-5 alkoxy, amino, morpholino), amino which may be substituted with C1-5 alkyl; neighboring 2 groups of X1-X4 may be bonded to each other to be C1-5 oxyalkylene], N:CX5CX6:CX7 (X5-X7 = H, halo, C1-5 alkoxy, amino which may be substituted with C1-5 alkyl), CX8:NCX9:CX10 (X8-X10 = any group given for X5-X7), N:CX11CX12:N (X11, X12 = H, C1-5 alkyl), W:CX13NX14 (W = N, CX15, X13-X15 = H, C1-5 alkyl), CX16:CX17O (X15, X17 = H, C1-5 alkyl); R1 = H, halo, (halo)phenyl, C1-5 (phenyl)alkyl, C1-5 alkoxy which may be substituted with CO2H or C1-5 alkoxycarbonyl, OH, amino which may be substituted with C1-5 alkyl or C1-5 alkanoyl; R2 = CR3R4R5 [R3, R4 = H, halo, pyridyl, pyridazinyl, (C3-8 cycloalkyl)-C1-5 alkyl, etc.]; R5 = OH, C1-5 alkyl, C1-5 alkoxycarbonyl, C1-5 alkanoyloxy, CO2H, etc], their hydrates, pharmacol. acceptable salts, optically-active isomers, racemates, and diastereomer mixts. are prepared I are useful for prophylactic and/or therapeutic agents for diseases due to acceleration of tyrosine kinase activity, e.g. as antitumor agents, immunosuppressants, platelet aggregation inhibitors, antiatherosclerotics, inflammation inhibitors, etc. Et2NCMe2C.tplbond.CH was treated with EtMgBr and the resulting grignard reagent was treated with 4-chloro-2-phenylquinazoline (preparation given) to give I (R1 = Ph, R2 = CMe2NEt2, AB = CH:CHCH:CH) (II). This was dissolved in Et2O and treated with HCl/EtOAc to give II.HCl. IC50 values of this salt against EGF receptor tyrosine kinase activity and growth of human nasopharyngeal carcinoma KB cells were 14 μM and 0.89 μM, resp.